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TITLE: Promoter-based Theranostics for Prostate Cancer

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13. SUPPLEMENTARY NOTES

14. ABSTRACT

We created new molecular-genetic expression vectors for efficient, non-invasive diagnosis and targeted radiopharmaceutical therapy of prostate cancer (PC). The diagnosis vector consists of the tumor-specific PEG-promoter (PEG-Prom) and cDNA of human chorionic gonadotropin β chain (βhCG) as a reporter. We showed that transfection of the diagnostic vector to PC cells successfully produced detectable βhCG in the media by over-the-counter pregnancy kit and ELISA. We also showed that systemic, non-viral delivery of the vector to mice bearing human metastatic PC tumors produced detectable βhCG in serum and urine of the animals. The therapeutic vector has the PEG-Prom and HSV1-tk as a therapeutic gene. We also developed this therapeutic vector into clinically compatible version to comply with FDA regulation for later clinical transition. Mice with micrometastatic PC treated with [^{211}At]FAAU following systemic administration of the clinical vector showed significant delay in tumor development compared with untreated control. Healthy mice treated with the same therapeutic dose of [^{211}At]FAAU did not show any toxicity for 1 year.

15. SUBJECT TERMS
tumor-specific promoter, molecular-genetic imaging, radiotherapy, human chorionic gonadotropin β chain (βhCG), herpes simplex virus 1 thymidine kinase (HSV1-tk)

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INTRODUCTION: The major goal of the project is to develop a platform technology for detection and therapy of prostate cancer (PC) based on induced cancer-specific expression of reporter or therapeutic proteins.

1. **KEYWORDS:** tumor-specific promoter, molecular-genetic imaging, radiotherapy, human chorionic gonadotropin β chain (βhCG), herpes simplex virus 1 thymidine kinase (HSV1-tk)

2. **ACCOMPLISHMENTS:**
   - **a. What were the major goals of the project?**
     - **1)** To generate plasmids for tumor-specific expression of diagnostic gene (βhCG) and therapeutic gene (HSV1-tk)
     - **2)** To test efficiency of PEG-prom driven βhCG as new diagnostic marker *in vitro* and *in vivo*
     - **3)** To test therapeutic efficacy of PEG-Prom driven HSV1-tk with [^{211}At]FAAU *in vitro* and *in vivo*
   - **b. What was accomplished under these goals?**

A. New diagnostic system for prostate cancer

Encouraged by our previous success in molecular-genetic imaging of human metastatic cancer in animal model (REF), we proposed to develop new diagnostic system for PC by systemically delivering a plasmid formulated with nanoparticle for *in vivo* transfection to express human chorionic gonadotropin β chain (βhCG) under the control of tumor-specific promoter. βhCG is expressed certain human cancers and can be easily detected by simple urine or blood tests. We have successfully generated expression vectors capable of expression of the cancer-specific progression elevated gene 3 promoter (PEG-Prom) driven βhCG. When we transfected PC3 and LNCaP prostate cancer cells with the vector, we were able to detect human βhCG in the culture media using βhCG ELISA assay, indicating that the PEG-Prom was capable of expressing soluble and secreted βhCG in prostate cancer cell lines (**Fig. 1**). In order to test this *in vivo*, we have developed a mouse model of human metastatic prostate cancer that develops tumors within liver, kidney, and bone after

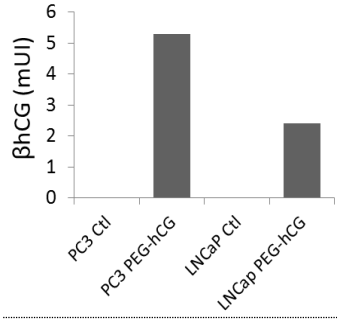

Figure 1. PEG-Prom driven hCG was successfully expressed and secreted into the media from PC3 and LNCaP cells.

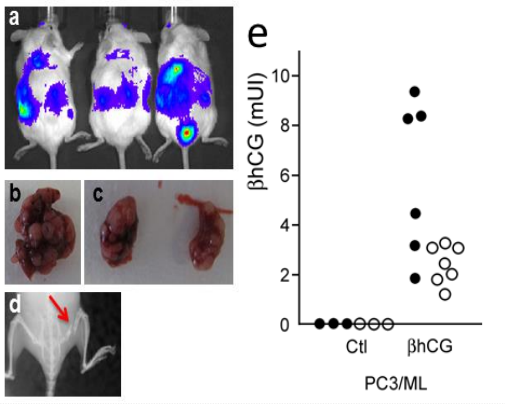

Figure 2. PEG-Prom driven hCG was successfully expressed and secreted to serum and urine of Experimental Metastatic mouse model of human prostate Cancer. (a) Bioluminescent images of mice with metastatic model. (b) Liver metastasis. (c) Kidney metastasis. (d) Lytic bone metastasis (arrow). (e) Serum (closed circles) and urine (open circles) level of βhCG. Each circle represents one mouse.

Figure 3. Detection of PEG-Prom driven (cancer specific) production of βhCG using a commercial urine pregnancy test. Note faint line of detection on right. This indicates feasibility of universal cancer detection using a simple and available kit.

intravenously injecting one million PC3/ML cells tagged with firefly luciferase (fLuc) to NOD/SCID/IL2rγ^{null} (NSG) mice (**Fig. 2**). This model starts to develop detectible metastatic lesions three weeks after the injection and dies at around the 6th week due to metastatic disease. The tumor expresses fLuc for non-invasive tracking of metastatic tumor development. We injected pPEG-βhCG vectors formulated with *in vivo* jetPEI for systemic delivery to our metastatic PC-bearing mice and healthy mice as a control group. Forty eight hours after the injection of the nanoplex, we collected blood and urine from each mouse and measured the level of human βhCG. We were able to detect soluble βhCG in both serum and urine of tumor bearing mice whereas there were no detectable βhCG from healthy mice (**Fig. 2e**). We have even shown that we could detect βhCG from the urine of tumor-bearing mice using a commercial pregnancy test (**Fig. 3**).

B. Creation of clinically compatible theranostic vectors

Our success in animal applications of molecular-genetic approach led us to human transpation of this new platform technology. Our current research grade vectors, however, are not suitable for human application for reasons described below. In order for these vectors to be readily translated into human application we designed clinically compatible vectors equipped with following features: a) CpG-free vector backbones and reporters, b) Neomycin/Kanamycin resistant selection marker, c) Scaffold/Matrix Attachment Region (S/MAR) sequences and d) small size. Majority of expression vectors used for research contains sequences from bacterial origin. These bacterial sequences and mammalian promoters often rich in unmethylated 2'-deoxyribo (cytidine-phosphateguanosine) (CpG) dinucleotides. When introduced to vertebrate animals, unmethylated CpG sequences can be recognized by Toll-like Receptor (TLR9) followed by acute induction proinflammatory cytokines such as IL-6, IFNγ, TNFα, and IL-12, which could be lethal. We took advantage of the CpG-free vector from the InvivoGen containing CpG-free R6K gamma origin of replication, CpG-free polyadenylation signal, CpG-free Neomycin/Kanamycin resistant gene and CpG-free multiple cloning sites. Using the Neomycin/Kanamycin resistant gene is important as US FDA only allows it for clinical use. Ampicillin, most widely used antibiotic is prohibited due to hyper-reactivity of some patients to beta lactam antibiotics. S/MAR sequence enables plasmid DNA act as an artificial chromosome resulting in prolonged existence of the plasmid over multiple cell divisions. It is also reported that the size of the plasmid affect transfection efficiency and keeping the minimal (less than 5.5 kb) would be critical to maintain optimal transfection efficiency. We also used CpG-free cDNA of

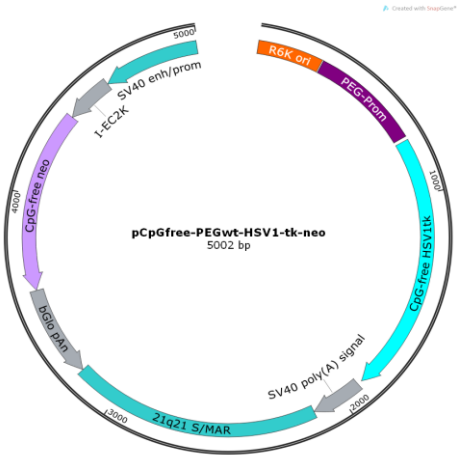

Figure 4. Diagram of the pCpGfree-PEGwt-HSV1-tk-neo vector.

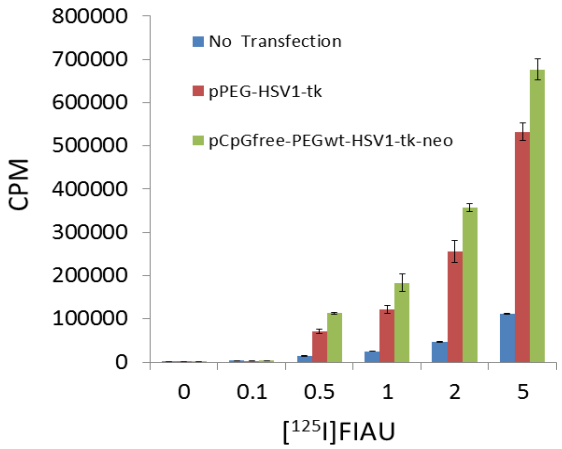

Figure 5. pCpGfree-PEGwt-HSV1-tk-neo vector expressed functional thymidine kinase in human PC cell line.

	IL-12 (sensitivity: 7.8pg/mL)			TNF- α (sensitivity: 10.9pg/mL)			IFN-γ (sensitivity: 9.3pg/mL)		
	Non-injected	pPEG-fLuc	PEGwt	Non-injected	pEPG-fLuc	PEGwt	Non-injected	pEPG-fLuc	PEGwt
Mouse1	ND	1202.9	1.6	ND	30.3	21.2	ND	23108.9	6091.1
Mouse2	ND	593.9	ND	ND	39.9	30.2	ND	17320.0	8520.0
Mouse3	ND	747.0	ND	ND	41.8	26.7	ND	15293.3	5848.9
Mouse4	ND	989.4	ND	ND	53.2	38.8	ND	22882.2	5633.3
Mouse5	ND	972.4	4.6	ND	49.4	27.3	ND	20404.4	5293.3
Average		901.1			42.9	28.8		19801.8	6277.3
STDEV		235.6			8.9	6.5		3437.8	1287.5

HSV1-tk for the vector to create full CpG-free vector except for the sequence of the PEG-Prom (**Fig. 4**, pCpGfree-PEGwt-HSV1-tk-neo).

The pCpGfree-PEGwt-HSV1-tk-neo vector was capable of expressing functional thymidine kinase when transfected to human PC cell line PC3 as evidenced by *in vitro* radio-uptake assay using [^{125}I]FIAU as HSV1-tk substrate (**Fig. 5**). In addition, cells transfected with the CpGfree-PEG-tk vector exhibited better uptake of [^{125}I]FIAU compared with cells with regular CpG-containing vector, pPEG-HSV1-tk (**Fig. 5)**

Encouraged by the successful expression of PEG-Prom-driven functional thymidine kinase in human PC cell line, we further created advanced version of plasmids with CpG-free and CpG-reduced PEG-Prom. Most of mammalian promoters have CpG sequences and spontaneous methylation of these CpG sequences within promoters causes rapid decline of reporter expression due to epigenetic silencing. Removing CpG sequences from expression vectors showed reduced immune response and prolonged expression of a reporter. We found 42 CpG sequences in the PEG-prom and created two additional vectors with a) complete CpG-free PEG-Prom and b) vector with reduced CpG sequences leaving CpG sequences reside in transcription binding sites. Both CpG-free and CpG-reduced PEG-Proms exhibited reduced promoter activities in tested cells indicating these CpG-sequences in the wild type PEG-Prom are essential for its activity (data now shown). We chose the pCpGfree-PEGwt-HSV1-tk-neo vector for our further studies.

C. Determining the level of induction of proinflammatory cytokines upon injection of CpG-containing and CpG-reduced plasmid

To evaluate further the clinical compatibility of the CpG-reduced vector we tested whether there were significant differences between the CpG-containing original vector and the CpG-free vector with PEGwt with respect to inducing inflammatory reactions when systemically injected into immune-competent mice. We formulated both plasmids with commercial *in vivo*-jetPEI and injected them into CD-1 mice intravenously. CpG-reduced plasmids showed significant reductions in induction of acute inflammatory cytokines (IL-12, TNF-α, and IFN-γ) in serum compared with those for the CpG-containing, research grade vector pPEG-fLuc (**Table 1**).

Table 1. Induction of inflammatory cytokines (ND: not detected)

D. Testing the therapeutic efficacy of PEG-HSV1-tk + [^{211}At]FAAU in metastatic prostate cancer

We used metastatic PC3/ML cells to express fLuc stably for non-invasive monitoring of disease progression in a murine model (**Fig. 2**). We tested the efficacy of molecular-genetic therapy (i.e. systemic delivery of a vector for PEG-Prom-driven HSV1-tk expression followed by administration of 740 kBq of [^{211}At]FAAU, the HSV1-tk substrate labeled with a therapeutic α-emitter, targeting metastatic lesions. We used *in vivo*-jetPEI for systemic delivery. We tested two versions of the expression vector, CpG-containing research grade vector (l-PEI TK) and CpG-reduced clinical vector (l-PEI CfTK). Animals treated with both vectors showed a significant delay in tumor development compared with non-treated animals (**Fig. 6**). Animals treated only with [^{211}At]FAAU did not show any therapeutic efficacy (data not shown). In addition, the CpG-reduced vector exhibited enhanced therapeutic efficacy relative to the CpG-containing vector. We performed a long-term toxicity study of [^{211}At]FAAU (up to 1.48 MBq) with immunocompetent mice. No mice demonstrated any abnormality in weight, CBC, creatinine, and ALT for up to 1 year (data not shown).

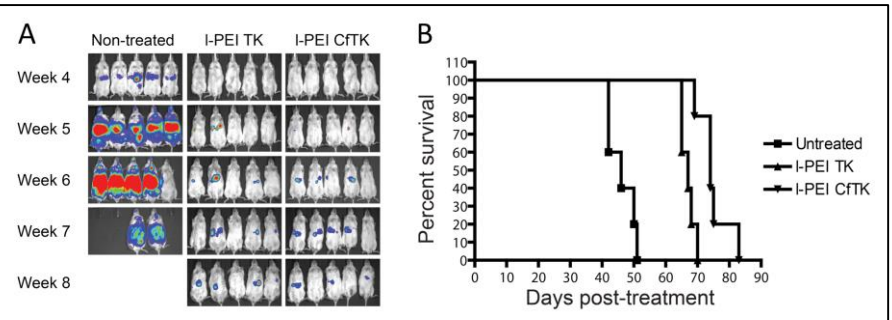

Figure 6. PEG-Prom-driven HSV1-*tk* in combination with [^{211}At]FAAU showed significant tumor growth delay in a micrometastatic model of prostate cancer. A. Bioluminescent images of mice. B. Kaplan-Meier curve showing survival time after treatment. *P* = 0.0017.

c. **What opportunities for training and professional development has the project provided?**
Co-investigator Dr. Minn was supported to attend the annual meeting of the Society for Nuclear Medicine and Molecular Imaging in 2015.

d. **How were the results disseminated to communities of interest?**
The results presented in this report will be published in high-impact peer-reviewed scientific journal.

e. **What do you plan to do during the next reporting period to accomplish the goals?**
   i. Nothing to Report.

3. IMPACT:

a. **What was the impact on the development of the principal discipline(s) of the project?**
The present research results demonstrate successful application of utility of the molecular-genetic imaging approach into simple, non-invasive diagnostic and effective therapy. For diagnostic application, we showed that our hypothesis to use βhCG as a reporter for easy detection using over-the-counter pregnancy test kit has worked with mice model of human PC. We also successfully combined tumor-specific expression of HSV1-tk and treatment with therapeutic radio-labeld substrate [^{211}At]FAAU for treating mice model of metastatic PC.

b. **What was the impact on other disciplines?**

Our successful development of clinically compatible expression vector backbone can be adopted to other gene therapy applications other than PC for their clinical translation.

c. **What was the impact on technology transfer?**
Our invention of the tumor-specific promoter driven reporter system for imaging human cancer has been licensed to the Canter Targeting Systems Inc. for clinical translation of the approach.

d. **What was the impact on society beyond science and technology?**
No current impact on society to report. Upon successful clinical translation of the research will provide the PC patients with safe, non-invasive ways to detect the cancer and more options for treating aggressive metastatic PC in the future.

4. CHANGES/PROBLEMS:
No changes or problems to report

5. PRODUCTS:
No product to report

6. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

- **What individuals have worked on the project?**
  - No change
- **Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?**
  - Martin Pomper

Ended

Title: Promoter-based Theranostics for Prostate Cancer
Time commitments: 0.60 calendar months
Supporting Agency: W81XWH-13-PCRP-EHDA PC131771
Grants Contact: TBN
PI: Pomper
Performance Period: 09/15/2014-09/14/2015
Level of Funding: $75,000
Description of Goals: the ultimate clinical goals of this project: (1) a commercially available nanoparticle that has been in clinical trials will contain a gene promoter that will turn on only when it comes into contact with PCa; (2) the gene promoter will start producing secreted β-hCG, which can be detected with a urine pregnancy test, effectively turning a pregnancy test strip into a device for cancer detection; (3) one can switch out the secreted β-hCG for HSV1-TK and then inject the patient with imaging or therapeutic versions of FIAU to enable imaging or therapy of PCa – potentially in asymptomatic men.
Aim 1: Generate PEG-βhCG and AEG-βhCG plamids
Aim 2: Generate PEG- βhCG and AEG-HSV1-TK plasmids
Aim 3: Testing of plasmids generated in vitro and in vivo

Title: Promoter-driven Molecular Radiotherapy for Prostate Cancer
Time Commitments: 0.42 calendar months
Supporting Agency: Prostate Cancer Foundation
Grants Contact: Howard Soule, Chief Science Officer
PI: Pomper
Performance Period: 10/15/2012-10/15/2015
Level of Funding: $500,000
Description of Goals: We propose a radical, new method for treating both primary and metastatic prostate cancer (PCa).
Aim 1: Optimize the nanoparticle delivery system with respect to the key features of toxicity, long circulation stability and high in vivo transfection efficiency.
Aim 2: Construct a PEG-Prom-driven gene that will place (strept)/avidin on the surface of PCa cells.
Aim 3: To use our existing PEG-Prom-driven HSV1-TK system to enable sequestration of an α-particle emitter, [211At]FAAU, specifically within PCa to afford selective tumor cell kill.

Title: New ALDH-Based Imaging Agents for Stem Cells
Time Commitments: 0.18 calendar months
Supporting Agency: MSCRC-TEDCO RFA-MD-12-2
Grants Contact: Dan Gincel, 410 715-4172, E-Mail:dgincel@marylandtedco.org
PI: Pomper
Role: Co-investigator
Performance Period: 06/30/2012-06/29/2014
Level of Funding: $100,000
Description of Goals: The ultimate goal is to be able to detect what are arguably the most malignant aspects of the tumor, i.e., the CSCs, in addition to developing a new way to track transplanted human stem cells without the need for introduction of a reporter gene.
Aim 1: Synthesis of a small library of radiolabeled and fluorescent substrates for ALDH
Aim 2: Evaluation of the ALDH substrates synthesized in Aim 1 in relevant CSC models.
Aim 3: Imaging of CSC positive tumors in relevant animal models.

New

Title: Study to Assess Single and Multiple Intravenous Doses of LY3002813 in Patients
Time Commitments: 0.12 calendar months
Supporting Agency: Shin Nippon Biomedical Laboratories
Grants Contacts: Christopher Hickey, Vice President Business Development, (443) 685-5800, chickey@snbl-cpc.com
PIs: Pomper
Performance Period: 04/08/16 - 04/07/17
Level of Funding: $ 925,149
Description of Goals: To perform human brain PET imaging as a biomarker to assess the safety, tolerability, pharmacokinetics, and pharmacodynamics of single and multiple intravenous doses of LY3002813 in patients with mild cognitive impairment due to Alzheimer's disease or mild to moderate Alzheimer's disease

Title: Systemic Radionuclide Therapy Targeted to VEGF Receptors in Tumor Vasculature
Time Commitments: 0.24 calendar months
Supporting Agency: HHSN261201500073C Backer-SIB Tech/ Pomper-JHU)
Grants Contacts: TBN
PIs: Pomper
Performance Period: 09/01/2015 - 05/31/2018
Level of Funding: $61,728.00
Description of Goals: To develop a radiotherapeutic agent that targets VEGF receptors to treat cancer

Title: Plasmid Selection and Characterisation
Time Commitments: 1.20 calendar months
Supporting Agency: Cancer Targeting Systems, Inc.
Grants Contacts: TBN
PIs: Pomper
Performance Period: 02/01/2016 - 07/31/2017
Level of Funding: $416,271.00
Description of Goals: To assess the functionality, yield and specificity of CpG-free and nanoplasmid variants of the CTS construct (backbone_PEG-3-HSV1-tk) to inform and hence enable selection of the optimal variant for further development, suitable for use on the clinic and to provide characterization data.

Title: PSMA-associated PET imaging of CAR T cells
Time Commitments: 0.12 calendar months
Supporting Agency: Juno Therapeutics
Grants Contacts: TBN
PIs: Pomper
Performance Period: 11/01/2015 – 10/31/2016
Level of Funding: $95,492
Description of Goals: To develop a PSMA-based molecular-genetic imaging system for tracking T cells

Title: Cancer-Specific Nanoparticle-Mediated Gene Therapy to Treat Hepatocellular Carcinoma
Time Commitments: 0.45 calendar months
Supporting Agency: NIH R01EB022148
Grants Contacts: TBN
PIs: Green
Performance Period: 04/01/16 - 03/31/21
Level of Funding: $250,000
Description of Goals: The primary goal is to develop new non-viral, PBAE nanoparticle-based gene delivery system to treat hepatocellular carcinoma.

- IL Minn

Ended

Title: Promoter-based Theranostics for Prostate Cancer
Time commitments: 0.60 calendar months
Supporting Agency: W81XWH-13-PCRP-EHDA PC131771
Grants Contact: TBN
PI: Pomper
Performance Period: 09/15/2014-09/14/2015
Level of Funding: $75,000
Description of Goals: the ultimate clinical goals of this project: (1) a commercially available nanoparticle that has been in clinical trials will contain a gene promoter that will turn on only when it comes into contact with PCa; (2) the gene promoter will start producing secreted β-hCG, which can be detected with a urine pregnancy test, effectively turning a pregnancy test strip into a device for cancer detection; (3) one can switch out the secreted β-hCG for HSV1-TK and then inject the patient with imaging or therapeutic versions of FIAU to enable imaging or therapy of PCa – potentially in asymptomatic men.
Aim 1: Generate PEG-βhCG and AEG-βhCG plamids
Aim 2: Generate PEG- βhCG and AEG-HSV1-TK plasmids
Aim 3: Testing of plasmids generated in vitro and in vivo

Title: Promoter-driven Molecular Radiotherapy for Prostate Cancer
Time Commitments: 0.42 calendar months
Supporting Agency: Prostate Cancer Foundation
Grants Contact: Howard Soule, Chief Science Officer
PI: Pomper
Performance Period: 10/15/2012-10/15/2015
Level of Funding: $500,000
Description of Goals: We propose a radical, new method for treating both primary and metastatic prostate cancer (PCa).
Aim 1: Optimize the nanoparticle delivery system with respect to the key features of toxicity, long circulation stability and high in vivo transfection efficiency.
Aim 2: Construct a PEG-Prom-driven gene that will place (strept)/avidin on the surface of PCa cells.
Aim 3: To use our existing PEG-Prom-driven HSV1-TK system to enable sequestration of an α-particle emitter, [^{211}At]FAAU, specifically within PCa to afford selective tumor cell kill.

Title: Treatment of Diabetic Retinopathy with Human iPSC-Derived Vascular Progenitors
Time Commitments: 0.6 calendar months
Supporting Agency: Maryland Stem Cell Research Fund
Grants Contact: Dan Gincel, 410 715-4172, E-Mail:dgincel@marylandtedco.org
PI: Park
Role: Co-Leader
Performance Period: 6/1/2014-5/31/2016
Level of Funding: $100,000

Description of Goals: The ultimate goal is to be able to successfully engraft iPSC-derived vascular progenitor cells to regenerate vasculature damaged by diabetes.

Title: New ALDH-Based Imaging Agents for Stem Cells
Time Commitments: 0.18 calendar months
Supporting Agency: MSCRC-TEDCO RFA-MD-12-2
Grants Contact: Dan Gincel, 410 715-4172, E-Mail:dgincel@marylandtedco.org
PI: Pomper
Role: Co-investigator
Performance Period: 06/30/2012-06/29/2014
Level of Funding: $100,000
Description of Goals: The ultimate goal is to be able to detect what are arguably the most malignant aspects of the tumor, i.e., the CSCs, in addition to developing a new way to track transplanted human stem cells without the need for introduction of a reporter gene.
Aim 1: Synthesis of a small library of radiolabeled and fluorescent substrates for ALDH
Aim 2: Evaluation of the ALDH substrates synthesized in Aim 1 in relevant CSC models.
Aim 3: Imaging of CSC positive tumors in relevant animal models.

New
Title: High-Specificity Imaging Agents for Aggressive Prostate Cancer
Time commitments: 1.80 calendar months
Supporting Agency: NIH/NCI (Renewal) R01CA134675
Grants Contact: Leota Hall; Program Official; 240-276-6449; halle@gmail.nih.gov
PI: Pomper
Role: Co-Investigator
Performance Period: 12/1/2014-11/30/2019
Level of Funding: $443,885
Description of Goals: The goals of this project are to leverage existing but untested agents and to develop new agents for imaging PC, with a focus on aggressive, localized disease.
Aim 1: Imaging of patients with biopsy-proved primary PC with DCFPyL-PET with subsequent correlation of PET signal with histopathology at prostatectomy for PSMA expression, Gleason score and other markers
Aim 2: Synthesis of select PSMA-targeted imaging agents that (a) encompass a new scaffold to engender superior affinity and pharmacokinetics; (b) are hetero-bivalent (HtBv), homing to a rationally chosen co-target (in addition to PSMA); or, (3) enable detection with MR through signal amplification
Aim 3: Development and testing of new agents for imaging the PC microenvironment

Title: PSMA Directed Imaging of Prostate Cancer Focus on Androgen Receptor Dynamics
Time Commitments: 2.4
Supporting Agency: NIH/NCI U01CA183031
Grants Contacts: Yantian Zhang; Program Official; 240-276-5980; Yantian.zhang@nih.gov
PIs: Pomper/Deweese
Performance Period: 11/01/2014-10/31/2016
Level of Funding: $496,642

Description of Goals: The overall goal is to validate at least two positron-emitting, PSMA-targeted imaging agents clinically so that they can be used to full advantage in supporting existing and emerging therapies for a spectrum of patients suffering from PCa.

Aim 1. To image treatment-naïve patients with localized-locally advanced primary PCa using DCFBC-PET/magnetic resonance imaging, and correlate signal with that on MR concurrently obtained, as well as with tumor grade, PSMA expression and androgen receptor (AR) signaling before and after two months of neoadjuvant androgen deprivation (ADT).

Aim 2. To image patients with CRPC using DCFBC-PET/MR and correlate findings with bone and soft tissue biopsy.

Aim 3. To image patients with CRPC with DCFBC-PET/MR and correlate with standard 99mTc-based bone scan to guide stereotactic body radiation treatment (SBRT) in patients with oligometastatic disease.

Aim 4. Imaging CRPC with the second-generation, PSMA-targeted PET agent, [18F]DCFPyL.

Title: Specific Molecular Imaging Agents for Clear Cell Renal Cell Carcinoma Diagnosis
Time Commitments: 0.6
Supporting Agency: NIH/NCI R03CA197470
Grants Contacts: Houston Baker, PO, 240-276-5908, bakerhou@mail.nih.gov; Jacquelyn Boudjeda, GMS, 240-276-6312, boudjedaj@mail.nih.gov
PIs: Yang
Performance Period: 07/01/15-06/30/17
Level of Funding: $50,000
Description of Goals: The primary goal is to develop small molecule imaging agents specifically targeting clear cell renal cell carcinoma using carbonic anhydrase IX as a target.